

# Research within the scope of the Swiss Human Research Act in 2016/2017

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## Overarching report on

Sub-project 1: Descriptive statistics on research within the scope of the Swiss Human Research Act

Sub-project 2: Survey of researchers on implementation of the Human Research Act

Sub-project 3: Characteristics of jurisdictional inquiries submitted to the cantonal ethics committees between July and December 2017

Basel, 12 December 2018

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**Version corrected May 2019**

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## List of abbreviations

<b>BASEC</b>	Business Administration System for Ethics Committees
<b>CCER</b>	Cantonal Research Ethics Committee, Geneva
<b>CER-VD</b>	Cantonal Research Ethics Committee, Vaud
<b>CE-TI</b>	Cantonal Ethics Committee, Ticino
<b>ClinO</b>	Ordinance on Clinical Trials in Human Research
<b>CTU</b>	Clinical Trial Unit
<b>EKNZ</b>	Ethics Committee of Northwestern and Central Switzerland
<b>EKOS</b>	Ethics Committee of Eastern Switzerland
<b>FOPH</b>	Federal Office of Public Health
<b>HRA</b>	Human Research Act
<b>HRO</b>	Ordinance on Human Research with the exception of Clinical Trials
<b>KEK-BE</b>	Cantonal Ethics Committee, Bern
<b>KEK-ZH</b>	Cantonal Ethics Committee, Zurich

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## Summary

**Introduction:** The Human Research Act (HRA) regulates the ethical, scientific and legal requirements that apply to research projects involving human beings in Switzerland, and entered into force on 1 January 2014. In November 2015 the ethics committees launched their electronic Business Administration System for Ethics Committees (BASEC). All the ethics committees' approval and notification processes have been processed via this system since 1 January 2016. Since its launch, the BASEC system has therefore obtained detailed and standardised information for the whole of Switzerland on research projects that fall within the scope of the HRA. These data can be analysed to build up a complete picture of human research in Switzerland since 2016. At the same time, BASEC data can be used to obtain information on approval procedures, e.g. processing times. Since 2017, clarifications of responsibility, i.e. queries from researchers as to whether their research project falls under the scope of the HRA and therefore needs to be submitted to an ethics committee for review, have also been recorded and processed using BASEC. This opens up the possibility of including research projects that are at the limit of the scope in the analysis of human research. Furthermore, the researchers who have submitted a research project or clarification of responsibility via BASEC constitute an appropriate cohort that can provide information on the functioning of the human research legislation and the BASEC system.

**Aims and methodology:** This project, which was commissioned by the Federal Office of Public Health and swissethics as part of federal policy research to evaluate the HRA, consisted of three complementary sub-projects. The aim of this report was to integrate the main results of the three sub-projects ("Descriptive statistics on research within the scope of the Human Research Act (HRA)", "Survey of researchers on the implementation of the HRA" and "Characteristics of the jurisdictional inquiries submitted") in one overview. The goal of sub-project 1 was to provide a statistical analysis and description of the research projects submitted via BASEC in 2016 and 2017, as well as an analysis of the duration of ethics committee approval procedures. Sub-project 2 used a systematic online survey of all researchers who submitted a research project via BASEC in 2017 to elicit the experiences and assessments of researchers regarding the HRA, the authorisation procedures of approval authorities and the BASEC system. Finally, the goal of sub-project 3 was to pinpoint the "threshold" of the HRA by analysing all jurisdictional inquiries submitted via BASEC in the second half of 2017 and to gauge existing uncertainties among researchers with regard to human research legislation. It also sought to obtain information on how researchers rate the submission process, the clarification provided by ethics committees and the disclosed outcomes of the clarification of responsibility.

**Results:** In 2016 and 2017 a total of between 2,100 and 2,300 research projects were submitted to the responsible ethics committees for review in Switzerland, and just over 2,100 were approved in 2017. There were some differences in the approaches taken by Switzerland's seven ethics committees. In the survey, more than 70% of researchers were in favour of more standardisation between Swiss ethics committees, while almost 30% explicitly advocated a centralised ethics committee.

Clinical trials accounted for around a quarter of all approved research projects. Nearly 40% of clinical trials tested medicinal products, 27% medical devices and 32% other interventions, such as surgical procedures and behavioural therapies. Combinations of medicinal products and medical devices, such as drug-eluting stents and transplant products, were rarely studied (0.4%), and there were no cases of trials with gene therapies or transplants as interventions in

2017. The majority of clinical trials on medicinal products were international, industry-led multicentre studies involving as yet unauthorised drugs; however, most clinical trials on medical devices or other interventions investigated standard treatments in monocentre, researcher-led studies. Studies involving persons that did not constitute clinical trials and further use studies made up the bulk of the approved research projects (35% and 40% respectively) and were predominantly monocentre, researcher-led studies. The majority (55%) of the further use studies approved in 2017 used uncoded data or biological material, although informed consent had only been obtained from the person concerned or had been requested by the ethics committees in fewer than 40% of projects. This means that for more than 60% of further use studies, the ethics committees permitted application of Article 34 of the Human Research Act, under which further use of health-related personal data or biological material can be made without informed consent if it would be disproportionately difficult or impossible to obtain consent and provided further conditions are met. On the whole, the process for submitting research projects and jurisdictional inquiries in BASEC and communication with ethics committees and Swissmedic were rated very positively by researchers.

More than two thirds of researchers felt that the key aspects of the HRA and its ordinances, such as clinical trials, risk categorisation, data protection and research involving vulnerable persons were properly managed. Compared with regulations in other countries, a quarter of researchers claimed that Swiss regulations were more burdensome in the sense of more laborious for researchers; a quarter believed the Swiss regulations were not more laborious for researchers and 50% did not express an opinion. Representatives of industrial studies were much more positive in this regard (saying that Swiss regulations were not more laborious) than representatives of researcher-led studies. Fifteen per cent of researchers claimed they had been excluded from international trials on one or more occasions on account of regulatory “obstacles” in Switzerland (almost exclusively representatives of researcher-led studies). Finally, almost 15% of researchers stated that they had explicitly decided to conduct a project abroad and not in Switzerland for various reasons, the most common of which was a lack of available trial subjects.

Two thirds of respondents felt that many researchers are not familiar with the HRA and its ordinances. Indeed, in 25% of jurisdictional inquiries we found contradictory information that suggested gaps in researchers’ knowledge. Researcher uncertainty regarding the scope and terminology of the HRA mainly concerned questions on “generalisable knowledge” and “anonymised data”.

**Limitations:** The analyses in this project were limited to data available in the BASEC system or data that were collected in online surveys. We did not contact any researchers to complete missing information or to clarify information that was unclear. A comparison of the characteristics of researchers who took part in the survey and those who did not was not possible because the only data we had available for this purpose were from the survey. Nevertheless, we assumed that the sample was sufficiently representative as the distribution of projects conducted by researchers who took part in the survey largely corresponded to the distribution of all research projects in 2017. Information on investigated diseases have so far been lacking in BASEC, which means no statements could be made on what type of studies were conducted into which diseases in Switzerland.

**Conclusions:** This project gives an overview of human research in Switzerland for 2016 and 2017 and provides a revealing insight into the views and experiences of researchers with regard to the HRA, the enforcement authorities and the BASEC system. On account of the positive evaluation of the HRA by researchers, on the whole we do not see a need to make

comprehensive changes to the legislation. In some cases, rectifications appear appropriate: the frequent application of Article 34 in further use studies, which was only intended for exceptional cases, suggests that stricter implementation of the regulations on this point would place a heavy burden on research practice. There needs to be greater consistency between the legal intention and feasibility in research practice here. The conceptual uncertainties noted by researchers relating to HRA concepts such as “generalisable knowledge” and “anonymised data” could be tackled in the legal text itself by providing more information and explanations, including concrete, illustrative examples, or through simpler wording and clearer formulations. The vast majority of researchers felt that efforts should be made to further harmonise the authorisation procedures of ethics committees. Automating the recording of processing times rather than manual entries by individual ethics committees in the BASEC system could encourage further harmonisation of processes. Information on investigated diseases should also be included in BASEC.

## 1. Introduction

The Federal Act on Research involving Human Beings (Human Research Act, HRA) and the related implementing ordinances have been in force since 1 January 2014. The HRA regulates the ethical, scientific and legal requirements that apply to research projects involving human beings. The primary aim of the Act is to protect the dignity, privacy and health of human beings involved in research, while creating favourable conditions for research involving human beings, safeguarding research quality and ensuring transparency.

The cantonal research ethics committees play a key role in this context as they review every research project that falls within the scope of the HRA before it is conducted to check it meets the legal requirements and can thus be approved. In November 2015, the ethics committees launched an electronic project submission and administration system, the Business Administration System for Ethics Committees (BASEC). All the ethics committees' approval and reporting procedures have been processed via this system since 1 January 2016. Since its launch, the BASEC system has therefore obtained detailed and standardised information for the whole of Switzerland on research projects that fall within the scope of the HRA. These data can be analysed to build up a complete picture of human research in Switzerland since 2016. At the same time, the BASEC data can be used to provide information on the approval procedures (type, processing times, type of decisions, etc.). Since 1 July 2017, clarifications of responsibility, i.e. enquiries from researchers as to whether their research project falls under the scope of the HRA and therefore needs to be submitted to an ethics committee for review, have also been recorded and processed via BASEC throughout Switzerland. This opens up the possibility of including research projects that are at the limit of the scope in the analysis of human research.

In addition, researchers who have submitted a research project via BASEC constitute an appropriate cohort that can provide information on the functioning of the human research legislation and the BASEC system. Applicants can be surveyed in a specific and timely manner about their research project and their experience in dealing with the human research legislation and how the legislation is enforced by the approval authorities.

## 2. Aims

The aim of this report was to integrate the main results of the three sub-projects (“Descriptive statistics on research within the scope of the Swiss Human Research Act (HRA)”, “Survey of researchers on implementation of the HRA” and “Features of submitted clarifications of responsibility”) in one overview.

The aims of the individual sub-projects were the following:

**Sub-project 1:** To analyse and describe the research projects submitted via BASEC in 2016 and 2017 within the scope of the HRA, as well as the length of the ethics committees' approval procedures.<sup>1</sup>

**Sub-project 2:** To carry out a systematic survey of all researchers who submitted a research project via BASEC in 2017 on their assessment of various aspects of the HRA, their experience with the approval procedures of the ethics committees and Swissmedic where applicable, as well as their experience with the BASEC submission process.<sup>2</sup>

**Sub-project 3:** To analyse and describe the jurisdictional inquiries submitted via BASEC between 1 July and 31 December 2017 in order to gain more detailed information about the uncertainties of researchers with regard to the HRA and research projects at the limit of the scope of the HRA. This was accompanied by a systematic survey of researchers who submitted a clarification of responsibility within the stated timeframe in order to gauge their assessment of the submission process, clarification by the ethics committee and the disclosed outcome.<sup>3</sup>

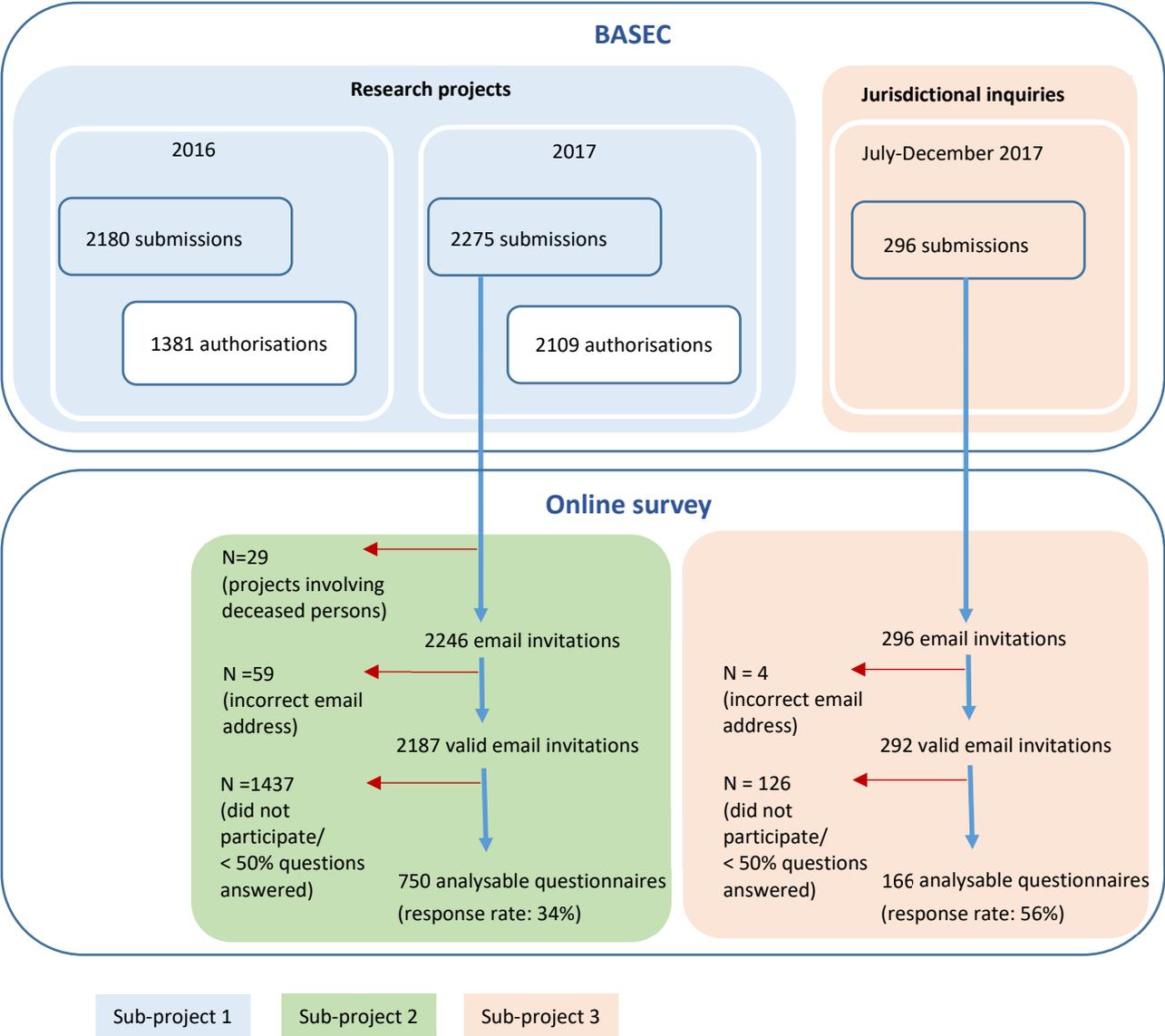
### 3. Methods

For a detailed description of the methods used, we refer to the relevant methodology sections in the three sub-project reports. The following section therefore focuses on those aspects of the applied methods that we regard as important in understanding and evaluating the study results.

To be able to describe the research projects submitted in 2016 and 2017 in more detail (**sub-project 1**), the relevant data were exported from the BASEC system by swissethics by arrangement with the presidents of the ethics committees and made available to our research team for analysis. Project-specific data (e.g. study type, risk category) were entered directly in the BASEC system by the submitting party and if necessary modified during the course of the approval procedure by an approval authority (ethics committee or Swissmedic). Data on the stages in the approval procedure of ethics committees were entered directly in BASEC for each research project by ethics committee staff. Two analysis sets were created for both 2016 and 2017: one based on all research projects submitted in the relevant calendar year and one based on all research projects approved in the relevant calendar year (**Figure 1**). The analysis set relating to submitted research projects per year roughly reflects the workload of ethics committees, while the analysis set relating to approved research projects provides information on human research projects conducted in Switzerland.<sup>1</sup>

To survey researchers on the HRA and on their experiences with the BASEC system (**sub-project 2**), a detailed online survey was developed. Based on information from interviews with researchers and employees of Clinical Trial Units (CTUs), an initial questionnaire was drawn up and then developed in an iterative process in collaboration with representatives of the Federal Office of Public Health (FOPH) and swissethics. A pre-final version was programmed using the Sphinx Online Manager software (SphinxSurvey, Erding, Germany) and tested online on a selected group of researchers. The final online questionnaire ultimately consisted of a first part, which focused on the submission process in the BASEC system, and a second part, which was geared towards researchers' experiences and evaluations of the HRA as a whole. This second part also contained specific questions depending on project type. For example, researchers who had submitted an application for a clinical trial in risk category B or C under the HRA and thus required approval from Swissmedic, were also asked about their experiences with Swissmedic's approval procedure. Overall there were three different versions of the second part of the questionnaire depending on the project category: (i) projects requiring an additional approval from Swissmedic, (ii) projects involving persons that do not require an additional approval from Swissmedic, i.e. clinical trials in risk category A or observational studies, and (iii) further use studies, i.e. projects involving existing health-related personal data or biological material. Projects involving deceased persons or embryos/foetuses were not taken into account in the survey as the numbers of such projects were very low. Researchers working on 2,187 projects submitted via BASEC in 2017 were therefore invited to complete the

online survey with a valid email address (Figure 1). The response rate was 34%. We assume the sample is largely representative as the distribution of projects conducted by researchers who took part in the survey largely corresponded to the distribution of all research projects in 2017. A comparison of researcher characteristics was not possible as we only had data from the survey for this purpose and none from BASEC.<sup>2</sup>



**Figure 1:** Schematic overview of the relationship between sub-projects 1-3

The analysis of jurisdictional inquiries(**sub-project 3**) took into account all enquiries submitted in BASEC with the associated documents in the researcher-selected category “jurisdictional inquiries/clarifications of responsibility” between 1 July and 31 December 2017. All the relevant information from the existing documentation in BASEC was extracted in an iteratively adapted data form and qualitatively analysed. In addition, all researchers who submitted a clarification of responsibility during the specified period were invited to take part in a short online survey on their experiences and assessments of the submission and processing of clarifications of responsibility. The response rate was 56% (Figure 1).<sup>3</sup>

The statistical software R version 3.5.1 was used for data processing and analyses in sub-projects 1 and 2. In sub-project 3 we used STATA version 13.0 for the quantitative analyses.

## 4. Results

### 4.1 Overview of research projects submitted in 2016/2017 and ethics committee approval procedures

A total of 2,180 research projects in 2016 and a total of 2,275 research projects in 2017 were submitted to the responsible ethics committees for review (**Table 1**). Just under 70% of research projects were evaluated as part of a “simplified procedure” in both years, i.e. the approval decision was taken by only three members of an ethics committee. In both years, fewer than 12% of submitted research projects were approved immediately without any additional requirements in the first review process. For more than 80% of research projects (future) approval was subject to requirements or conditions.<sup>1</sup>

**Table 1:** Research projects submitted in 2016 and 2017 with decisions, based on information from ethics committees<sup>1</sup>

		Year			
		2016		2017	
		n	%col	n	%col
First decision	Approved <sup>1</sup>	239	11.0	265	11.6
	Approved with charges <sup>2</sup>	626	28.7	622	27.3
	Not approved, conditions <sup>3</sup>	1166	53.5	1238	54.4
	Declined	38	1.7	23	1.0
	Non-consideration <sup>4</sup>	73	3.3	71	3.1
	Pending first decision <sup>5</sup>	38	1.7	56	2.5
Final decision	Approved <sup>6</sup>	1943	89.1	1885	82.9
	Declined	41	1.9	22	1.0
	Non-consideration	71	3.3	69	3.0
	Withdrawn	53	2.4	24	1.1
	Pending final decision <sup>7</sup>	72	3.3	275	12.1
Review procedure	Ordinary <sup>8</sup>	406	18.6	400	17.6
	Simplified <sup>9</sup>	1507	69.1	1537	67.6
	Presidential <sup>10</sup>	229	10.5	282	12.4
	Pending first decision	38	1.7	56	2.5
Total number of submissions		2180	100.0	2275	100.0

<sup>1</sup> Projects already approved in the first review process.

<sup>2</sup> Charges: The projects are approved but with charges.

<sup>3</sup> Conditions: These projects are not approved until the conditions are addressed.

<sup>4</sup> Non-consideration: Research not covered by the HRA.

<sup>5</sup> Information missing: The status information was missing at the time of the report generation.

<sup>6</sup> Note that this includes projects approved both in the index year as well as in the subsequent year(s) until the time of the data export (April 2, 2018).

<sup>7</sup> Pending at export date (April 2, 2018). 48.0% of the pending projects were submitted in the last quarter of the reporting year.

<sup>8</sup> Decision taken at full commission meeting by at least seven members of the ethics committee, as per the provisions of Art. 5, OrgO-HRA.

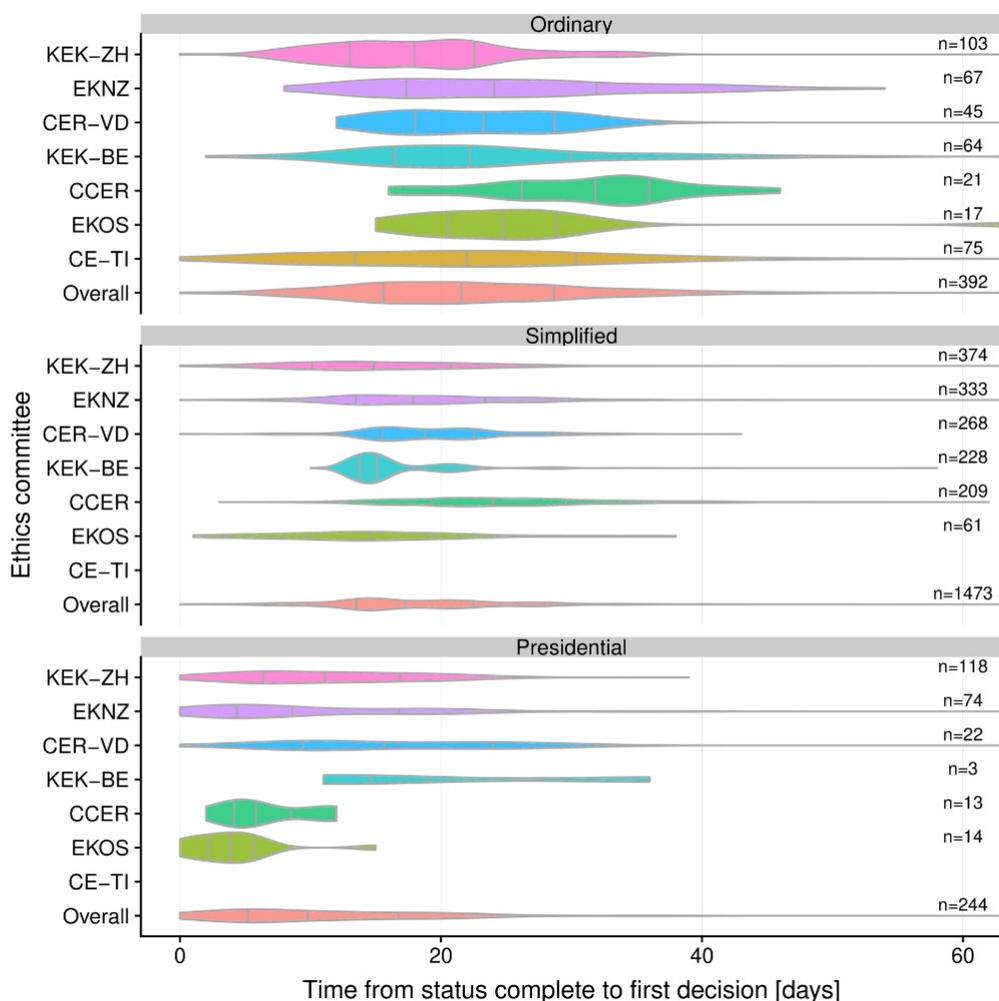
<sup>9</sup> Decision taken by three members of the ethics committee, as per the provisions of Art. 6 OrgO-HRA.

<sup>10</sup> Decision taken by the president or vice-president of the ethics committee, as per the provisions of Art. 7 OrgO-HRA.

In the researcher survey, the vast majority (over 85%) felt the requirements and conditions of ethics committees were fundamentally justified, both in general and regarding ethical and legal issues. On the whole, ethics committees and Swissmedic only rarely modified the study type or risk classification originally specified by researchers and if they did, researchers usually received a clear and coherent explanation from the approval authority.<sup>2</sup>

A differentiated view of the approval procedures employed by the seven ethics committees in Switzerland showed that their approaches differ to some extent. For example, in the first review process in 2016 and 2017, the Ethics Committee of Northwestern and Central Switzerland (EKNZ) favoured approval with conditions (around two thirds of decisions), while the cantonal ethics committees of Zurich (KEK ZH) and Bern (KEK BE) decided in 75% of cases on “no

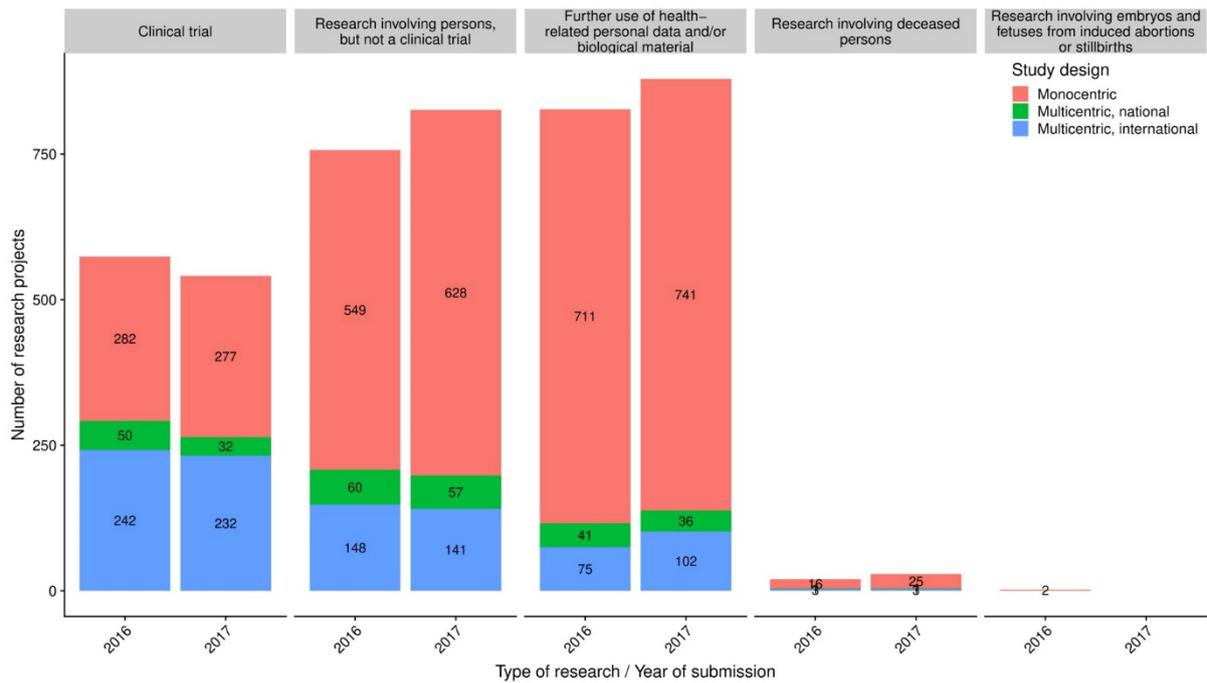
approval yet, conditions must be fulfilled first". The Ticino Ethics Committee (CE-TI) decided on virtually all submitted research projects in the "ordinary procedure" in plenary, while the other ethics committees ruled on most research projects in the "simplified procedure" or in the "presidential procedure".<sup>1</sup> Differences were also apparent between the individual ethics committees in terms of processing times, for example from submission of the complete dossier to the first decision (**Figure 2**).<sup>1</sup>



**Figure 2:** Violin diagram showing processing times of ethics committees from submission of a complete dossier to first decision, grouped by type of procedure (2017)<sup>1</sup>

In the survey the vast majority (over 70%) of researchers expressed a wish for greater standardisation between Switzerland's ethics committees, with almost 30% explicitly advocating a central ethics committee for the whole of Switzerland.<sup>2</sup>

Most of the research projects submitted in 2016 and 2017 involved the further use of existing health-related personal data or biological material (Human Research Ordinance (HRO), Chapter 3) and studies involving persons that do not constitute clinical trials (HRO, Chapter 2) (**Figure 3**).<sup>1</sup> Clinical trials (Ordinance on Clinical Trials in Human Research (ClinO)) made up around one quarter of all research projects submitted in 2016 and 2017. Research projects involving deceased persons and projects involving embryos/foetuses were rare. In all project categories monocentre studies predominated, with the exception of clinical trials, where about the same number of monocentre and multicentre projects were submitted. In the case of a multicentre design, the research projects were mostly international.<sup>1</sup>



**Figure 3:** Comparison of research projects submitted in 2016 and 2017, grouped by study design<sup>1</sup>

#### 4.2 Overview of research projects approved in 2016/2017

A total of 1,381 research projects were approved by ethics committees in Switzerland in 2016 and a total of 2,109 in 2017.<sup>1</sup> This difference can be explained by the fact that the use of BASEC has only been mandatory since the beginning of 2016, which means that all projects that were submitted before the introduction of BASEC but were only approved in 2016, are not registered in BASEC. The absolute numbers of approved projects in 2016 are therefore not comparable with those in subsequent years. However, a comparison of the shares of approved research projects regarding various characteristics such as project type, study design and project initiator showed a high level of consistency between 2016 and 2017. We also noted a high level of concordance of project characteristics between submitted research projects (**Figure 3**) and approved research projects (**Table 2**). By way of example, we therefore limit ourselves to research projects that were approved in 2017 in the following more detailed examination.<sup>1</sup>

**Table 2:** Approved research projects 2017<sup>1</sup>

Type of research	Research details	Risk cat.	Study design										Initiator			
			Total		Mono		Multi CH		Multi Int.		Industry		Investigator			
			N	%col	n	%row	n	%row	n	%row	n	%row	n	%row		
Clinical trial (ClinO)	Medicinal products (ClinO Art 19)	A	20	10.2	11	55.0	4	20.0	5	25.0	2	10.0	18	90.0		
		B	41	20.9	14	34.1	7	17.1	20	48.8	11	26.8	30	73.2		
		C	135	68.9	15	11.1	6	4.4	114	84.4	108	80.0	27	20.0		
	All	196	100.0	40	20.4	17	8.7	139	70.9	121	61.7	75	38.3			
	Medical devices (ClinO Art 20)	A	96	70.1	67	69.8	2	2.1	27	28.1	22	22.9	74	77.1		
		C	41	29.9	23	56.1	3	7.3	15	36.6	24	58.5	17	41.5		
		All	137	100.0	90	65.7	5	3.6	42	30.7	46	33.6	91	66.4		
	Other clinical trials (ClinO Art 61)	A	136	81.9	103	75.7	14	10.3	19	14.0	4	2.9	132	97.1		
		B	30	18.1	25	83.3			5	16.7	1	3.3	29	96.7		
		All	166	100.0	128	77.1	14	8.4	24	14.5	5	3.0	161	97.0		
	Combination drugs/devices	A	4	44.4	2	50.0			2	50.0	2	50.0	2	50.0		
		C	5	55.6	1	20.0			4	80.0	4	80.0	1	20.0		
		All	9	100.0	3	33.3			6	66.7	6	66.7	3	33.3		
	Transplant products (ClinO Art 21)	C	4	100.0	3	75.0			1	25.0	1	25.0	3	75.0		
		All	4	100.0	3	75.0			1	25.0	1	25.0	3	75.0		
	Gene therapy (ClinO Art 22)	All	0													
	Transplantation (ClinO Art 49)	All	0													
	All	All	512	100.0	264	51.6	36	7.0	212	41.4	179	35.0	333	65.0		
Research w/ persons (HRO Chapter 2)	A	697	96.8	529	75.9	55	7.9	113	16.2	57	8.2	640	91.8			
	B	23	3.2	18	78.3	2	8.7	3	13.0			23	100.0			
	All	720	100.0	547	76.0	57	7.9	116	16.1	57	7.9	663	92.1			
Further use (HRO Chapter 3)	n.a.	854	100.0	734	85.9	33	3.9	87	10.2	35	4.1	819	95.9			
Deceased, embryos (HRO Chapter 4+5)	n.a.	23	100.0	21	91.3			2	8.7	1	4.3	22	95.7			
Total number			2109	100.0	1566	74.3	126	6.0	417	19.8	272	12.9	1837	87.1		

Abbreviations: mono: monocentre studies; multi CH: multicentre studies in Switzerland; multi int: multicentre international studies; risk cat: risk category

As with submitted research projects, clinical trials made up around a quarter of approved research projects in 2017 (Table 2). Almost 40% of clinical trials tested medicinal products (Article 19 ClinO) and 27% tested medical devices (Article 20 ClinO); combinations of drugs and devices, such as drug-eluting stents and transplant products (Article 21 ClinO) were rarely studied (0.4%). There were no cases of gene therapy (Article 22 ClinO) or transplantations (Article 49 ClinO) as clinical trial interventions in 2017, while the remaining 32% of clinical trials studied interventions other than those mentioned, such as surgical procedures and behavioural therapies. As expected, most clinical trials involving medicinal products were international, industry-led multicentre studies on as yet unauthorised medicinal products. On the other hand, most clinical trials on medical devices or other interventions examined standard treatments in monocentre, researcher-led studies.<sup>1</sup>

Placebo-controlled, researcher-led clinical trials in risk category B or C, which require approval from Swissmedic in addition to the ethics committee, were rare overall (6%; 30 of 512 clinical trials). Some 15% of clinical trials were conducted on healthy volunteers and a further 15% on children or adolescents.<sup>1</sup>

More than 90% of the studies involving persons that did not constitute clinical trials (76% of which were monocentre studies), and over 95% of further use trials (86% of which were monocentre studies) were researcher-led (Table 2).<sup>1</sup> Of the further use trials approved in 2017, 80% were conducted using existing non-genetic health data and 20% using existing genetic data or biological material (Table 3).<sup>1</sup> The majority (55%) of further use studies approved in 2017 used uncoded data or biological material, although informed consent was only available or had been requested by ethics committees from the persons concerned for fewer than 40% of projects. This means that for more than 60% of further use studies, the ethics committees permitted application of Article 34 HRA, which allows researchers to make further use of “biological material or health-related personal data for research purposes in exceptional cases” in the absence of informed consent from the persons concerned if “it is impossible or

disproportionately difficult to obtain consent or to provide information on the right to dissent, or this would impose an undue burden on the person concerned; no documented refusal is available; and the interests of research outweigh the interests of the person concerned in deciding on the further use of his or her biological material and data”.<sup>1</sup>

**Table 3:** Characteristics of further use studies approved in 2017<sup>1</sup>

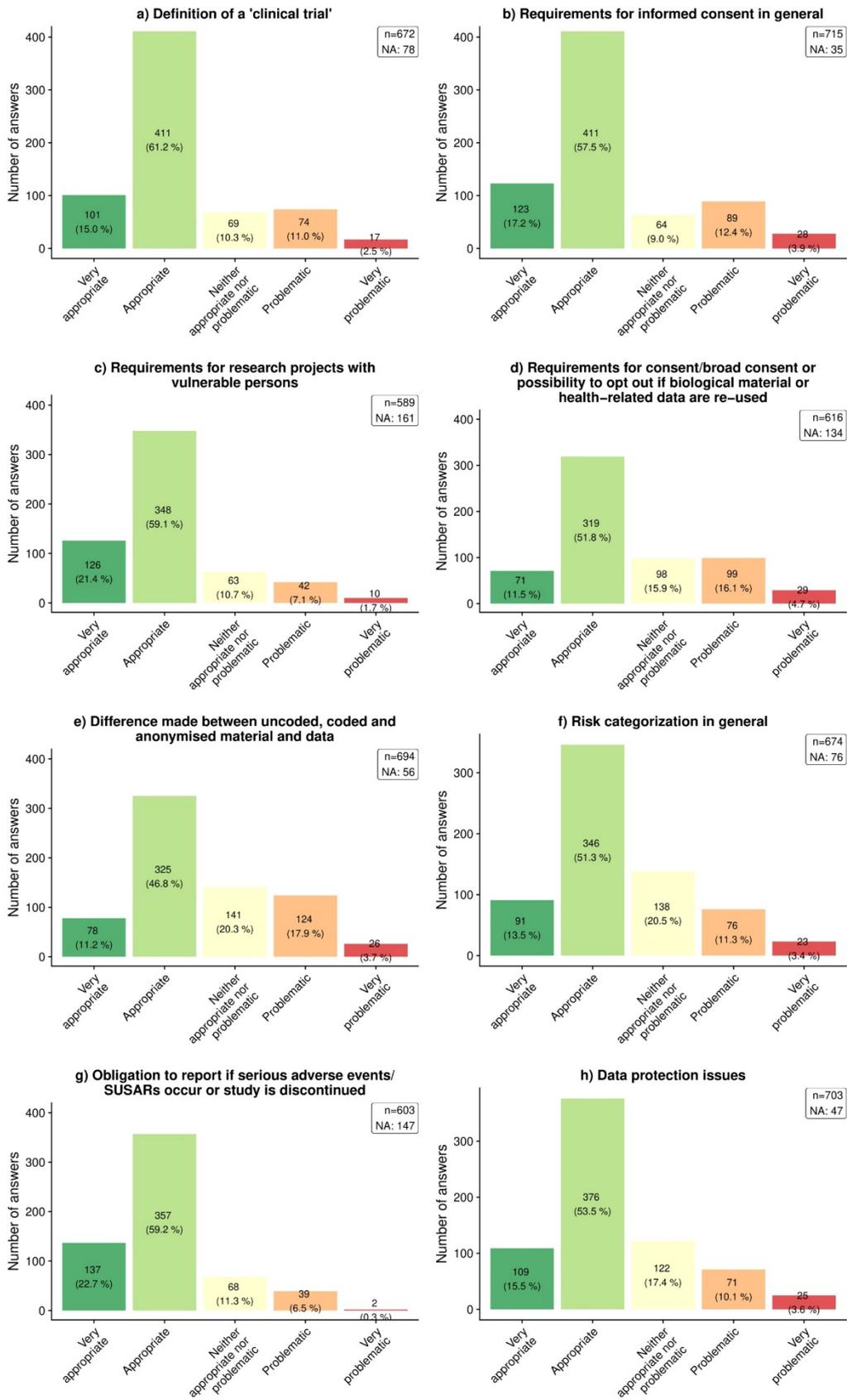
		n	%
Genetic data / biol. material	Yes	173	19.2
	No	726	80.8
Coding (HRO Art. 25-27)	Coded	412	45.8
	Open, non-coded	487	54.2
Consent (HRO Art. 28-32)	Prior consent exists	213	23.7
	Consent to be sought <sup>1</sup>	130	14.5
	No consent for some/all data (HRA Art 34)	556	61.8
Combined projects <sup>2</sup>	Further use project	854	95.0
	Part of clinical trial	16	1.8
	Part of non-clinical research project	29	3.2
Total number		899	100.0

<sup>1</sup> Consent to be sought means that the ECs do not apply HRA Art 34 and request the researchers to obtain the consent

<sup>2</sup> Combined projects: Research projects concerning a clinical trial (ClinO) or research involving persons according to HRO Chapter 2 that additionally include the 'further use' of existing data or biological material (HRO Chapter 3).

#### 4.3 Views of researchers on the HRA and its impact on research involving persons in Switzerland

In the survey, 40% of researchers agreed with the general statement that the HRA is a hindrance to human research. Concerning more specific key aspects of the regulation of human research, between two thirds and three quarters of researchers believed that these aspects were properly regulated in the HRA and its ordinances, however (**Figure 4**).<sup>2</sup>



**Figure 4:** Evaluation by researchers of the way in which key aspects of human research are regulated in the HRA and its ordinances<sup>2</sup>

Researchers who had submitted a research project involving human beings were specifically asked about the risk categorisation of trials introduced in the HRA (A,B,C). Two thirds of researchers agreed that the definitions of the categories were clear and straightforward, that the categorisation in itself was appropriate, that it was useful for protecting trial subjects, and that in the case of projects in risk category A, researchers could save a great deal of time and effort. Researchers felt that in clinical trials in risk category A the biggest simplification was that they did not require approval from Swismedic and did not have to document all the potential adverse effects of medicinal products or medical devices in the trial documentation. In addition, more than 80% of researchers who had submitted a clinical trial with the necessary Swissmedic approval in BASEC welcomed the recently-introduced parallel submission in BASEC and Swissmedic.<sup>2</sup>

With regard to the competitiveness of Switzerland as a location for research, a quarter of researchers felt the current legal regulations in Switzerland were more burdensome (in terms of involving more time and effort) than comparable regulations in other countries (25% explicitly disagreed with this and 50% expressed no opinion on this point). The majority of representatives of industrial trials (60%) did not consider the Swiss regulations to be more time-consuming (only 10% believed it was more time-consuming and 30% had no opinion on this point), whereas among representatives of researcher-led trials, 25% felt the Swiss regulations were more time-consuming, and only 20% believed they were less complex than regulations in other countries; 55% of representatives of researcher-led trials did not express an opinion on this point. In the group of researchers who felt the Swiss regulations were more complex, the proportion of further use studies was higher (40%) than in the group who did not note a difference compared with regulations in other countries (30%). Overall, 15% of researchers stated that they had been excluded from international trials on one or more occasions on account of regulatory “obstacles” since the introduction of the HRA (85% answered no to this question). Almost all those concerned had submitted researcher-led trials. Finally, nearly 15% of researchers said they had consciously decided to conduct a trial abroad rather than in Switzerland (more than 85% answered no to this question). Various reasons were given for this, including career-related or other personal reasons, as well as cost, time needed to obtain approval(s) and availability of trial subjects.<sup>2</sup>

#### 4.4 Uncertainty among researchers regarding the HRA and its scope

In the survey, two thirds of researchers agreed with the statement that “many researchers are not familiar with the HRA and its ordinances”.<sup>2</sup> Although the question was worded as a third party assessment, we can assume that researchers primarily drew on their own level of knowledge to answer this question. On the other hand, when researchers were asked whether in planning and developing their project they found it difficult to decide whether the project even fell under the scope of the HRA, which ordinance to apply and which was the appropriate risk category, 75% stated that this was either not the case or only to a very minor degree, and 25% found it somewhat to very difficult.<sup>2</sup> In the second half of 2017, a total of 218 jurisdictional inquiries concerning the applicability of the HRA were submitted in BASEC.<sup>3</sup> Around 1,100 research projects were submitted in BASEC for review and approval during the same period,<sup>1</sup> which equates to a ratio of jurisdictional inquiries to directly submitted projects of 1:5. The most common cause for uncertainty among researchers who submitted a clarification of responsibility was whether their research project would produce “generalisable knowledge” (Art. 3a HRA), followed by uncertainty around the use of “anonymised data” (Art. 3i HRA) (Table 4).<sup>3</sup>

**Table 4:** Concepts and specialist terms on the scope of the HRA where researchers were uncertain and therefore submitted a clarification of responsibility<sup>3</sup>

<b>Legal concepts causing difficulties in interpretation</b>	<b>Freq.</b>	<b>Percentage</b>
Uncertain whether the project would produce generalisable knowledge (Art. 3a HRA)	59	27.1
Uncertain whether the project would involve anonymised data (Art. 3i HRA)	43	19.7
Uncertain whether the project would involve health-related data (Art. 3f HRA)	22	10.1
Uncertain whether the project is about human diseases, body structure, or body functions (Art. 2 HRA)	20	9.2
Uncertain whether informed consent is required	11	5.1
Uncertain whether the research project is a clinical trial (Art. 3l HRA), including those who inquired about the applicable ordinance (ClinO or HRO)	10	4.6
Uncertain about import/export of biological material, genetic data or other health-related data (e.g. Art. 42 HRA)	3	1.4
Uncertain about further use of data, samples of an ongoing research project	2	0.9
Uncertain about the competence/jurisdiction of the cantonal or faculty EC	1	0.5
Uncertain about the applicability of the HRA or another law	1	0.5
No specific difficulty with a legal term identified	46	21.2
<b>Total</b>	<b>218</b>	<b>100</b>

In the researcher survey conducted within the scope of the analysis of clarifications of responsibility, almost 60% of researchers said they had no difficulties understanding the questions asked and terms used in the relevant form for clarifications of responsibility, and just under 25% said they had some problems understanding one or more questions.<sup>3</sup> In a comprehensive overview of the information submitted for each clarification of responsibility, we note that some 25% of requests for clarification contain contradictory information, which suggests gaps in researchers' knowledge. This most frequently concerned the question on the form as to whether the biological material or personal data used in the research project was irreversibly anonymised. Researchers often replied yes to this question, although they did not plan to work with anonymised data from the beginning of their project, but instead to anonymise the data themselves during the course of the project, or the code for the coded data used still existed.<sup>3</sup> One point worth mentioning here is that in the survey, only 15-20% of researchers said they had received help from CTUs or Contact Research Organisations (CROs) in developing the trial protocol or in submitting their research projects in BASEC.<sup>2</sup>

Research involving anonymised data or biological material does not fall under the scope of the HRA and is therefore not recorded using the BASEC system. In the survey of researchers who had submitted a clarification of responsibility, just under half stated that they had never worked with anonymised data, around a quarter said they sometimes worked with anonymised data, and 15% said they frequently worked with anonymised data (10% did not answer the question).<sup>3</sup> Researchers who frequently worked with anonymised data were typically very active (three or more research projects submitted in BASEC) and experienced (more than 10 years' experience in research).<sup>3</sup> In the survey of researchers who had submitted a further use study in BASEC, 50% considered research involving anonymised data or biological material less or not at all useful compared with research involving coded or uncoded data, and 50% considered it equally useful or even more useful.<sup>2</sup>

#### 4.5 Evaluation by researchers of BASEC processes, communications and competence of ethics committees and Swissmedic

In the survey, 58% of researchers rated the submission process in the BASEC system as good on the whole, and 18% as very good.<sup>2</sup> Between 60% and 75% of researchers described the process as clear, concise, convenient and appropriate. Sixty per cent of researchers said the submission did not take as long or took less time than expected, and 40% felt the submission took “a bit longer” to “much longer” than expected. Close to 90% of researchers found the number of documents to be uploaded in BASEC acceptable or were indifferent. Just under 60% of researchers said they contacted an ethics committee or swissethics once or more during the project submission process to ask questions or get advice. Around 40% of researchers whose project also required an application to Swissmedic contacted Swissmedic once or more to ask questions for get advice. Communication with ethics committees and Swissmedic was rated as good overall by 44% of researchers and as very good by 38%. The answers supplied by ethics committees to researchers’ questions were rated as clear, relevant and timely by the overwhelming majority of researchers. The responses from Swissmedic were also described by the vast majority as clear and relevant.<sup>2</sup>

As part of the survey, researchers were asked to evaluate various aspects that are typically considered by ethics committees when reviewing research projects in terms of their importance in the review and the competence of ethics committees in assessing these aspects. Researchers felt that ethics committees placed particular emphasis on protecting the rights and integrity of trial subjects, patient information and informed consent, and the fulfilment of requirements regarding coding and anonymisation of data (in each case more than 75% of researchers stated maximum or considerable importance). Meanwhile, the qualification and experience of research groups, the suitability of infrastructure at trial locations, sufficient funding and trial feasibility were seen as less important in the review (in each case fewer than 35% of researchers answered maximum or considerable importance). The competence of ethics committees was assessed very similarly to the individual aspects, e.g. high significance of patient information was associated with a high level of competence in this area.<sup>2</sup>

Eighteen per cent of researchers involved in projects that required both a submission in BASEC and Swissmedic noted inconsistent evaluations between an ethics committee and Swissmedic. These concerned, for example, the defined risk category or differing assessments of the study risk for pregnant women.<sup>2</sup>

Researchers gave the submission process for jurisdictional inquiries in the BASEC system a similarly positive rating as the submission of research projects described above. The “submission channel” for jurisdictional inquiries was not only used by researchers for these clarifications, but also in 25% of cases for direct requests for clarifications of responsibility and various other matters (for example notifications of amendments to trial protocols).<sup>3</sup> According to researchers, 88% of the research projects on which the jurisdictional inquiries were based were subsequently started or were scheduled to start. A closer look reveals that 99% of projects (111 of 112) that did not require approval from an ethics committee, and 80% of projects (36 of 45) that did require approval from an ethics committee went ahead. The overwhelming majority of researchers (93%) agreed with the results of the jurisdictional inquiries.<sup>3</sup>

## 5. Limitations

The main limitations of this report can be summarised as follows. The data underlying the three sub-projects were exclusively from two data sources: the BASEC system and the replies from researchers in the online surveys. This means that the evaluated information is mainly based on information from researchers and to a small extent in BASEC also on information from individual ethics committees. We did not check the existing information, nor did we contact any researchers or ethics committees to clarify or supplement any missing or unclear information. Incorrect or missing information did not pose a major problem for the statistical evaluation of the approved research projects (sub-project 1) as the relevant data were recorded in a standardised manner in BASEC and had been checked by the ethics committees to a certain extent. The information recorded in the BASEC system for jurisdictional inquiries was much less standardised, however (sub-project 3). In this area, the information in BASEC was often heterogeneous and not always available for the aspects that sub-project 3 was interested in. The response rates for the online surveys were satisfactory, at 34% for sub-project 2 and 56% for sub-project 3. The lower response rate for sub-project 2 is likely to be primarily related to the greater complexity of the survey and the significant extra time required of researchers. It was not possible to compare the characteristics of researchers who participated in the survey with those who did not as we only had the data from the survey available for this purpose, and no data from BASEC. Nevertheless, we assume that the sample is sufficiently representative as the distribution of projects conducted by researchers who took part in the survey largely corresponded to the distribution of all research projects in 2017. The statistical evaluation of BASEC data on submitted and approved research projects in 2016 and 2017 does not yet allow any meaningful analyses of developments in Switzerland's clinical research landscape over time. This will only be possible in subsequent years when complete data sets on approved research projects from several years are available. Information on investigated diseases have so far been lacking in BASEC, which means no statements could be made on what type of studies were conducted into which diseases in Switzerland.

## 6. Conclusions

This project, commissioned by the FOPH and swissethics as part of the evaluation of the HRA, consists of three complementary sub-projects, the results of which provide an overview of the human research landscape within the scope of the HRA, an assessment of the HRA and BASEC system by researchers, and an insight into the areas at the limit of the scope of the HRA through an analysis of jurisdictional inquiries. Owing to the positive evaluation of the HRA by researchers with regard to key aspects of the regulations on human research, we see no need for comprehensive amendments to the HRA or its ordinances. In terms of the workload for researchers generated by the HRA, representatives of industry-initiated trials were rather satisfied, whereas some representatives of researcher-initiated studies felt the HRA imposed a greater burden on researchers than regulations in other countries. We interpret the frequent application of Article 34 in further use studies (60% of cases)<sup>1</sup>, for example, as a way of ethics committees accommodating researchers to continue to allow retrospective studies to be conducted with justifiable effort using existing health-related personal data or biological material. Article 34 was only intended for exceptional cases, however. There is a divergence here between the legal intention and practical implementation, which should be aligned in future through relevant measures, for example a modification of the legal framework or more

stringent implementation by ethics committees. Most of researchers' conceptual uncertainties related to "generalisable knowledge" and "anonymised data"<sup>3</sup>. Here, too, there are essentially two options: more explanation of the core concepts and relevant specialist terms in the HRA, ideally using concrete, illustrative examples, or simpler wording and clearer formulations in the legal text itself.

According to researchers, when evaluating projects ethics committees pay particular attention to protecting the rights and integrity of trial subjects, patient information and informed consent, and fulfilment of the requirements regarding coding and anonymisation of data, and in these areas researchers felt the ethics committees also had a high level of competence.<sup>2</sup> From this we infer that the primary objective of the HRA (protection of trial subjects) is met in practice. The procedures of the individual ethics committees did and still do vary in some respects,<sup>1</sup> which researchers predominantly viewed as a shortcoming.<sup>2</sup> The vast majority of researchers advocated greater standardisation of the approval procedures, with almost 30% explicitly favouring a centralised ethics committee for the whole of Switzerland.<sup>2</sup> The Swiss ethics committees have been working on harmonising their processes for a number of years, and these efforts should continue based on the results of this study. Automating the recording of processing times instead of manual entries in the BASEC system by individual ethics committees could encourage further harmonisation of processes. Apart from that, researchers rated the BASEC submission process and communication with ethics committees as overwhelmingly positive.

We consider an annual evaluation of BASEC data to be an important tool to gauge developments in terms of number and type of studies in Swiss human research in a reliable and comprehensive fashion, and to create targeted incentives where appropriate. Information on the investigated diseases should also be included in BASEC. On account of the successful execution and comprehensive results of the researcher survey in sub-project 2, we would consider it sensible to repeat the survey at longer intervals (5-10 years) or following more substantial changes to the HRA or its ordinances.

## 7. References

- (1) Benkert P, Clinical Trial Unit Basel. Teilprojekt 1: Beschreibende Statistik der Forschung im Geltungsbereich des Schweizer Humanforschungsgesetzes (HFG). FOPH 2018
- (2) Von Elm E, Cochrane Schweiz. Teilprojekt 2: Befragung der Forschenden zur Umsetzung des HFG. FOPH 2018
- (3) Gloy V, Briel M, Basel Institute for Clinical Epidemiology and Biostatistics. Teilprojekt 3: Charakteristika von Zuständigkeitsabklärungen durch kantonale Ethikkommissionen Juli - Dezember 2017. FOPH 2018

## 8. Appendix

### Contributors

<b>Sub-project</b>	<b>Author(s)</b>	<b>Online survey</b>	<b>Analyses</b>
Sub-project 1 “Descriptive statistics on research within the scope of the Swiss Human Research Act”	Pascal Benkert, Thomas Zumbrunn, CTU Basel, Swiss Clinical Trial Organisation	Not applicable	Pascal Benkert
Sub-project 2 “Survey of researchers on implementation of the HRA”	Erik von Elm, Cochrane Schweiz, Viktoria Gloy (free text responses)	Ingrid Gilles und Federico Cathieni, ESOPE, Institute of Social and Preventive Medicine (IUMSP), Lausanne	Pascal Benkert
Sub-project 3 “Characteristics of jurisdictional inquiries submitted to cantonal ethics committees between July and December 2017”	Viktoria Gloy, Matthias Briel, Basel Institute for Clinical Epidemiology and Biostatistics (ceb)	Ingrid Gilles and Federico Cathieni, ESOPE, Institute of Social and Preventive Medicine (IUMSP), Lausanne	Viktoria Gloy

## **Corrigendum**

In an earlier version of this report, on page 18, Swissmedic's responses to requests from researchers were stated to be described as "significantly delayed" by a "large majority" of researchers. However, due to an inconsistent scale representation in the online survey of researchers, the data basis for this statement cannot be considered reliable. It is therefore not possible to quantify the true proportion of researchers who intended to indicate that Swissmedic's responses were "delayed".